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BANNER & WITCOFF, LTD.
1100 13th STREET, N.W.
SUITE 1200
WASHINGTON, DC 20005-4051

| EXAMINER | |
|---|---|
| WARE, DEBORAH K | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/568,765 | DANG ET AL. | |
| | Examiner | Art Unit | |
| | DEBBIE K. WARE | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-28 are presented for reconsideration on the merits.

### *Response to Amendment*

The amendment filed November 8, 2010, has been received and entered.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-18, 21-25 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating tumors with Clostridium novyi-NT strain, by deleting the lethal toxin gene on the phage episome, does not reasonably provide enablement for methods of treating tumors with any anaerobic bacterium, or any strain of C. novyi or C. sordellii, having a toxin gene deleted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Applicants' specification provides no disclosure of how to obtain them nor do any of the examples of the specification use any other strain than C. novyi-NT strain.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or

absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731,737, 8 USPQ2d1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir 1999).

Dang et al (reference cited on enclosed PTO-892 Form) sets forth that sequential treatment of C. novyi-NT spores, dolastatin-10 and MMC, resulted in dramatic effects on large tumors. However, Dang et al further set forth that results were "rarely" seen with C. novyi NT alone. (See page 5). Accordingly, one of skill in the art would be forced into excessive experimentation to identify a particular anaerobic bacterium having a toxin gene deleted, which can regress, slow or arrest the growth of a tumor.

Given the lack of guidance, lack of working examples, and the unpredictable nature of the invention, one of skill in the art would be forced into excessive experimentation in order to practice the instantly claimed invention.

***Response to Arguments***

Applicant's arguments filed November 8, 2010, have been fully considered but they are not persuasive. The argument that in Table 1, of col. 7, of USP 7344710, there is no indication that the others were totally unsuitable is not persuasive because at col. 7, lines 14-17, it is clearly indicated that other Clostridium strains did not exhibit the required phenotype when tested under identical conditions. Clearly Applicants are only

enabled for Clostridrium sordellii and Clostridium novyi. While the Examiner may not require Applicants to be limited to the specific strain C. novyi-NT, Applicants should limit the claims to at least the two species for which the art and disclosure supports as being able to express the required phenotype in order to practice and carry out the claimed invention. However, the Examiner has removed the written description and deposit rejection at this time, but the scope rejection is sustained over the broadest claims which do not require at least the species.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over previously cited Dang et al (USP 7344710) in view of **newly cited** Tito Fojo &

Paraskevi Giannakakou (Fojo et al), cited on previously enclosed PTO-1449 Form, and **newly cited** Helson et al (USP 5688517), **newly cited** Dewhirst et al (USP 5554638), US patents (USP) cited on enclosed PTO-892 Form.

Claims are drawn to method for treating tumors in a mammal and kit therefore. The method comprises administering to the mammal spores of a toxin-defective, anaerobic bacterium and administering to the mammal a microtubule stabilizing anti-tumor agent; whereby the tumor regresses or its growth is slowed or arrested. The kit for treating tumors has components that are in a divided or undivided container wherein the components are the spores of the bacterium, as required by the method, and stabilizing agent as required by the method. The bacterium is Clostridium novyi or Clostridium sordellii. The kit further comprises a nitric oxide synthetase (NOS) Inhibitor, and the agent can be taxol, taxotere, cephalomannine, epothilone B or taxane. The method requires administering steps which is performed serially and can be done intravenously, intratumorally

Dang et al. teach method and kit, therefore, for treating tumors in a mammal, comprising administering to the mammal spores of a toxin-defective, bacterium (anaerobic) and administering an anti-tumor agent to slow the tumor growth. Note col. 2, lines 1-25 and col. 4, lines 35-67, also see the entire abstract.

Fojo et al teach microtuble stabilizing agents to include taxane (p. 296, col. 1, lines 1-2), taxotere (p. 297, col. 1, line 18), taxol (p. 294, col. 1, line 13), taxane (p. 294, col. 1, line 11), and epothilone B (p. 294, col. 1, lines 13-14). These agents are used as anti-tumor agents, see introduction at p. 293.

Helson et al teach use of cephalomannine for treating tumor in a mammal, see abstract.

Dewhirst et al teach NOS Inhibitor is used as antitumor therapy to reduce tumor blood flow and oxygenation, see abstract. Further, it is administered with antitumor agents to enhance effectiveness of treating a tumor in a mammal. See abstract.

Claims differ from Dang et al in that microtuble stabilizing agents not used for combination bacateriolytic therapy for the treatment of tumors in mammals or in the kit, therefore.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace the agents disclosed by Dang et al with the agents disclosed by Fojo et al, Helson et al and to further select for use in the antitumor therapy of Dang et al the inhibitor disclosed by Dehwhirst et al because each have been used in the art for enhancement of effectiveness for the treatment of tumors. Each of the claim features are disclosed in the art. One of skill would have been motivated to replace the agents of Dang et al with the agents of Fojo et al, Helson and to further select the inhibitor as disclosed by Dewhirst et al because stabilizing agents suppress microtubule dynamics without increasing in polymer mass or formation of microtubule bundles. Clearly one of skill would have known that the microtubule stabilizing agents would provide successful results. To provide for kit, therefore, comprising these key components is clearly within the purview of an ordinary artisan. The claims are, therefore, rendered *prima facie* obvious over the cited prior art.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 20 of U.S. Patent No. 7344710 in view of Fojo et al, Helson et al and Dewhirst et al, all cited and discussed above.

The claims differ from the patented claims in that microtubule destabilizing agents are selected for use with the spores for combination bacteriolytic cancer therapy, and hence the only difference is scope per se, because the patented claims do not necessarily require microtubule destabilizing agents as the anti-tumor agents to be combined with the spores for combination bacteriolytic cancer therapy.

The '710 claims are drawn to administering spores of an isolated strain which is toxin-defective as claimed herein and also can administer an anti-tumor agent therewith, of which administering is carried out intravenously or intratumorally. Also the spores and agent are administered serially.

Each of Fojo et al, Helson et al and Dewhirst et al are discussed above.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to select replace the antitumor agent of '710 with the agents of the cited prior art to provide for the administering of the spores and microtuble stabilizing agents. One of skill in the art would have expected successful results and furthermore, would have been motivated as discussed above, to select for microtuble stabilizing agents. The agents are well known in the art and to select any one of these agents is well within the purview of an ordinary artisan. The claims are *prima facie* obvious over the patented claims.

***Response to Arguments***

Applicant's arguments filed November 8, 2010, have been fully considered but they are not persuasive. The argument that the claimed subject matter utilizes agents which have a diametriclaly opposite effect from the microtubule binding agents of Dang is noted. However, Fojo and Helson are both cited for their teachings of using microtuble stabilizing agents as claimed herein to treat tumors. The nexus between the art references is that each teaches the treating of tumors to be successfully carried out with the anaerobic bacterium spores and microtubule stabilizing agents. Thus, the prior art recognized at the time the claimed invention was made that each of these ingredients were successful for treating tumors. To combine these ingredients together in order to obtain the same effect for what each is well known in the art to be used for is prima facie obvious.

The principle operations of each of the references are not changed and the ingredients are functional equivalents useful for same purpose. The Dang reference does not constitute a teaching away per se simply because it uses different compounds for combining with the spores to obtain an overall anti-tumor effect. This would only be true if there was insufficient evidence that microtubule stabilizing agents can treat tumors. However, the secondary prior art clearly teach that these agents also have anti-tumor activity and properties, therefore, the selection of well known ingredients which are functional equivalents is prima facie obvious. These agents do not have an opposite effect for treating tumors which is what the claims are directed to in the instant case.

With respect to the argument regarding domination of a patent or application the obviousness double patenting is based upon the patented claims in view of secondary references. Therefore, obviousness double patenting rejection relies on the same premise for the rejection over prior art under 35 USC 103, and for these reasons as discussed above, the rejection under double patenting is sustained.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

All claims fail to be patentably distinguishable over the state of the art discussed above and cited on the previously enclosed PTO-892 and/or PTO-1449. Therefore, the claims are properly rejected.

The remaining references listed on the previously enclosed PTO-892 and/or PTO-1449 are cited to further show the state of the art.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DEBBIE K. WARE whose telephone number is (571)272-0924. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah K. Ware/
Deborah K. Ware
Primary Examiner
Art Unit 1651